

CLAIMS:

1. A peptide chemically modified with polyethylene glycol (PEG), including a sequence of 18 amino acids, wherein

said sequence of 18 amino acids is constituted from alternately arranged two hydrophobic sides and two hydrophilic sides in α -helix structural model depicted by Edmundson wheel plots,

one of said hydrophobic sides comprises 5 to 7 amino acids and 80 mole% or more of this side comprises hydrophobic amino acids,

one of said hydrophilic sides comprises 5 or 6 amino acids, and 80 mole% or more of this side comprises hydrophilic amino acids, and 50 mole% or more of this side comprises an amino acid selected from the group consisting of arginine and lysine,

the other of said hydrophobic sides comprises 2 to 4 hydrophobic amino acids, and

the other of said hydrophilic sides comprises 3 to 5 amino acids and 80 mole% or more of this side comprises hydrophilic amino acids.

2. A peptide chemically modified with PEG

according to claim 1 wherein said peptide comprises 20 or more amino acids in total; opposite ends of said peptide are N and C terminals; and any 18 consecutive amino acids in said peptide excluding the amino acids at opposite ends constitutes said sequence of 18 amino acids.

3. A peptide chemically modified with PEG according to claim 1 or 2 wherein the amino acids at the N and C terminals are each a hydrophilic amino acid.

4. A peptide chemically modified with PEG according to any one of claims 1 to 3 wherein said sequence of 18 amino acids is a sequence of any 18 consecutive amino acids in the following amino acid sequence:

X2-X3-X4-X5-X6-X7-X8-X9-X10-X11-X12-X13-X14-X15-X16-
X17-X18-X19-X20-X21-X22-X23-X24-X25-X26-X27-X28-X29-
X30-X31-X32-X33-X34-X35-X36,

provided that,

in each of "X4, X8, X11, X15, and X19", "X8, X11, X15, X19, and X22", "X11, X15, X19, X22, and X26", "X15, X19, X22, X26, and X29", and "X19, X22, X26, X29, and X33", at least 4 amino acids out of the 5 amino acids are a hydrophobic amino acid,

X3, X10, X12, X21, X28, and X30 are independently a

hydrophobic amino acid, a neutral hydrophilic amino acid, or a basic hydrophilic amino acid,

in each of "X2, X5, X9, X13, and X16", "X5, X9, X13, X16, and X20", "X9, X13, X16, X20, and X23", "X13, X16, X20, X23, and X27", "X16, X20, X23, X27, and X31", and "X20, X23, X27, X31, and X34", at least 4 amino acids out of the 5 amino acids are a neutral hydrophilic amino acid or a basic hydrophilic amino acid, at least 3 amino acids of which being arginine or lysine,

X6, X17, X24, and X35 are independently a hydrophobic amino acid, and

X7, X14, X18, X25, X32, and X36 are independently a neutral hydrophilic amino acid or a basic hydrophilic amino acid.

5. A peptide chemically modified with PEG according to any one of claims 1 to 4 wherein peptide moiety of said peptide chemically modified with PEG and including said sequence of 18 amino acids comprises the following amino acid sequence:

X1-X2-X3-X4-X5-X6-X7-X8-X9-X10-X11-X12-X13-X14-X15-
X16-X17-X18-X19-X20-X21-X22-X23-X24-X25-X26-X27-X28-
X29-X30-X31-X32-X33-X34-X35-X36-X37,

provided that

X1 and X37 are a hydrophilic amino acid,
in each of "X4, X8, X11, X15, and X19", "X8, X11, X15, X19, and X22", "X11, X15, X19, X22, and X26", "X15, X19, X22, X26, and X29", and "X19, X22, X26, X29, and X33", at least 4 amino acids out of the 5 amino acids are a hydrophobic amino acid,

X3, X10, X12, X21, X28 and X30 are independently a hydrophobic amino acid, a neutral hydrophilic amino acid, or a basic hydrophilic amino acid,

in each of "X2, X5, X9, X13, and X16", "X5, X9, X13, X16, and X20", "X9, X13, X16, X20, and X23", "X13, X16, X20, X23, and X27", "X16, X20, X23, X27, and X31", and "X20, X23, X27, X31, and X34", at least 4 amino acids out of the 5 amino acids are a neutral hydrophilic amino acid or a basic hydrophilic amino acid, at least 3 amino acids of which being arginine or lysine,

X6, X17, X24, and X35 are independently a hydrophobic amino acid, and

X7, X14, X18, X25, X32, and X36 are independently a neutral hydrophilic amino acid or a basic hydrophilic amino acid; and

wherein the sequence of amino acids X2 to X36 may include deletion, addition, insertion, or substitution as long as at least 18 amino acids are conserved in consecutive form.

6. A peptide chemically modified with PEG according to claim 5 wherein X1 to X37 are the following amino acids:

X1 is threonine,

X37 is serine,

X2, X5, X9, X20, X23, and X27 are independently arginine or lysine,

X3 and X21 are independently tyrosine, phenylalanine, serine, or arginine,

X4, X17, X22, and X35 are independently leucine,

X6, X15, X24, and X33 are independently leucine or isoleucine,

X7, X13, X25, and X31 are independently histidine or arginine,

X8 and X26 are independently proline,

X10 and X28 are independently serine, arginine, or leucine,

X11 and X29 are independently tryptophan or leucine,

X12 and X30 are independently valine, leucine, or serine,

X14 and X32 are independently glutamine, asparagine, or arginine,

X16 and X34 are independently alanine or arginine,

X18 is arginine, lysine, or serine,

X19 is leucine or threonine, and

X36 is arginine or serine; and

wherein the sequence of amino acids X2 to X36 may include deletion, addition, insertion, or substitution as long as at least 18 amino acids are conserved in consecutive form.

7. A peptide chemically modified with PEG according to any one of claims 1 to 6 wherein peptide moiety of said peptide chemically modified with PEG and including said sequence of 18 amino acids comprises any one of the amino acid sequences of SEQ ID NO: 1 to SEQ ID NO: 24.

8. A peptide chemically modified with PEG according to any one of claims 1 to 6 wherein peptide moiety of said peptide chemically modified with PEG and including said sequence of 18 amino acids comprises the amino acid sequence of SEQ ID NO: 16 or SEQ ID NO: 19.

9. A peptide chemically modified with PEG according to any one of claims 1 to 8 wherein PEG moiety of said peptide chemically modified with PEG and including said sequence of 18 amino acids has a molecular weight of

about 200 Da to about 100,000 Da.

10. A complex comprising a peptide chemically modified with PEG and including a sequence of 18 amino acids, and a substance which binds to said peptide wherein

said sequence of 18 amino acids is constituted from alternately arranged two hydrophobic sides and two hydrophilic sides in α -helix structural model depicted by Edmundson wheel plots,

one of said hydrophobic sides comprises 5 to 7 amino acids and 80 mole% or more of this side comprises hydrophobic amino acids,

one of said hydrophilic sides comprises 5 or 6 amino acids, and 80 mole% or more of this side comprises hydrophilic amino acids, and 50 mole% or more of this side comprises an amino acid selected from the group consisting of arginine and lysine,

the other of said hydrophobic sides comprises 2 to 4 hydrophobic amino acids, and

the other of said hydrophilic sides comprises 3 to 5 amino acids and 80 mole% or more of this side comprises hydrophilic amino acids.

11. A complex according to claim 10 wherein said

peptide comprises 20 or more amino acids in total; opposite ends of said peptide are N and C terminals; and any 18 consecutive amino acids in said peptide excluding the amino acids at opposite ends constitutes said sequence of 18 amino acids.

12. A complex according to claim 10 or 11 wherein the amino acids at the N and C terminals are each a hydrophilic amino acid.

13. A complex according to any one of claims 10 to 12 wherein said sequence of 18 amino acids is a sequence of any 18 consecutive amino acids in the following amino acid sequence:

X2-X3-X4-X5-X6-X7-X8-X9-X10-X11-X12-X13-X14-X15-X16-
X17-X18-X19-X20-X21-X22-X23-X24-X25-X26-X27-X28-X29-
X30-X31-X32-X33-X34-X35-X36,

provided that,

in each of "X4, X8, X11, X15, and X19", "X8, X11, X15, X19, and X22", "X11, X15, X19, X22, and X26", "X15, X19, X22, X26, and X29", and "X19, X22, X26, X29, and X33", at least 4 amino acids out of the 5 amino acids are a hydrophobic amino acid,

X3, X10, X12, X21, X28, and X30 are independently a

hydrophobic amino acid, a neutral hydrophilic amino acid, or a basic hydrophilic amino acid,

in each of "X2, X5, X9, X13, and X16", "X5, X9, X13, X16, and X20", "X9, X13, X16, X20, and X23", "X13, X16, X20, X23, and X27", "X16, X20, X23, X27, and X31", and "X20, X23, X27, X31, and X34", at least 4 amino acids out of the 5 amino acids are a neutral hydrophilic amino acid or a basic hydrophilic amino acid, at least 3 amino acids of which being arginine or lysine,

X6, X17, X24, and X35 are independently a hydrophobic amino acid, and

X7, X14, X18, X25, X32, and X36 are independently a neutral hydrophilic amino acid or a basic hydrophilic amino acid.

14. A complex according to any one of claims 10 to 13 wherein peptide moiety of said peptide chemically modified with PEG and including said sequence of 18 amino acids comprises the following amino acid sequence:

X1-X2-X3-X4-X5-X6-X7-X8-X9-X10-X11-X12-X13-X14-X15-
X16-X17-X18-X19-X20-X21-X22-X23-X24-X25-X26-X27-X28-
X29-X30-X31-X32-X33-X34-X35-X36-X37,

provided that

X1 and X37 are a hydrophilic amino acid,

in each of "X4, X8, X11, X15, and X19", "X8, X11, X15, X19, and X22", "X11, X15, X19, X22, and X26", "X15, X19, X22, X26, and X29", and "X19, X22, X26, X29, and X33", at least 4 amino acids out of the 5 amino acids are a hydrophobic amino acid,

X3, X10, X12, X21, X28 and X30 are independently a hydrophobic amino acid, a neutral hydrophilic amino acid, or a basic hydrophilic amino acid,

in each of "X2, X5, X9, X13, and X16", "X5, X9, X13, X16, and X20", "X9, X13, X16, X20, and X23", "X13, X16, X20, X23, and X27", "X16, X20, X23, X27, and X31", and "X20, X23, X27, X31, and X34", at least 4 amino acids out of the 5 amino acids are a neutral hydrophilic amino acid or a basic hydrophilic amino acid, at least 3 amino acids of which being arginine or lysine,

X6, X17, X24, and X35 are independently a hydrophobic amino acid, and

X7, X14, X18, X25, X32, and X36 are independently a neutral hydrophilic amino acid or a basic hydrophilic amino acid; and

wherein the sequence of amino acids X2 to X36 may include deletion, addition, insertion, or substitution as long as at least 18 amino acids are conserved in consecutive form.

15. A complex according to claim 14 wherein X1 to X37 are the following amino acids:

X1 is threonine,

X37 is serine,

X2, X5, X9, X20, X23, and X27 are independently arginine or lysine,

X3 and X21 are independently tyrosine, phenylalanine, serine, or arginine,

X4, X17, X22, and X35 are independently leucine,

X6, X15, X24, and X33 are independently leucine or isoleucine,

X7, X13, X25, and X31 are independently histidine or arginine,

X8 and X26 are independently proline,

X10 and X28 are independently serine, arginine, or leucine,

X11 and X29 are independently tryptophan or leucine,

X12 and X30 are independently valine, leucine, or serine,

X14 and X32 are independently glutamine, asparagine, or arginine,

X16 and X34 are independently alanine or arginine,

X18 is arginine, lysine, or serine,

X19 is leucine or threonine, and

X36 is arginine or serine; and
wherein the sequence of amino acids X2 to X36 may include deletion, addition, insertion, or substitution as long as at least 18 amino acids are conserved in consecutive form.

16. A complex according to any one of claims 10 to 15 wherein peptide moiety of said peptide chemically modified with PEG and including said sequence of 18 amino acids comprises any one of the amino acid sequences of SEQ ID NO: 1 to SEQ ID NO: 24.

17. A complex according to any one of claims 10 to 15 wherein peptide moiety of said peptide chemically modified with PEG and including said sequence of 18 amino acids comprises the amino acid sequence of SEQ ID NO: 16 or SEQ ID NO: 19.

18. A complex according to any one of claims 10 to 17 wherein said substance which binds to the peptide is a nucleic acid.

19. A complex according to any one of claims 10 to 18 wherein PEG moiety of said peptide chemically modified with PEG and including said sequence of 18 amino acids has

a molecular weight of about 200 Da to about 100,000 Da.

20. A method for producing the peptide chemically modified with PEG of any one of claims 1 to 9 comprising the step of reacting a peptide comprising said sequence of 18 amino acids with activated polyethylene glycol.

21. A peptide chemically modified with polyethylene glycol (PEG) which is produced by the method of claim 20.

22. A method for producing the complex of any one of claims 10 to 19 comprising the steps of

a) reacting a peptide comprising said sequence of 18 amino acids with activated polyethylene glycol (PEG), and

b) reacting the peptide chemically modified with PEG that is obtained in said a) with a substance which binds to said peptide.

23. A method for producing the complex of any one of claims 10 to 19 comprising the steps of

a) reacting a peptide comprising said sequence of 18 amino acids with a substance which binds to said peptide, and

b) reacting the reaction product of said peptide and

said substance which binds to said peptide with activated polyethylene glycol (PEG).

24. A complex of a peptide chemically modified with polyethylene glycol (PEG) and a substance which binds to said peptide, said complex being produced by the method of claim 22 or 23.

25. A carrier which is modified with the peptide chemically modified with PEG according to any one of claims 1 to 8.

26. A method for producing the carrier of claim 25 which is modified with the peptide chemically modified with PEG comprising the steps of

a) reacting a peptide comprising said sequence of 18 amino acids, or a peptide comprising said sequence of 18 amino acids and having cysteine attached to N or C terminal of the peptide, with activated PEG, and

b) reacting the reaction product of said a) with a carrier, or constructing a carrier by using the reaction product of said a) as a constituent.

27. A carrier which is modified with the peptide

chemically modified with PEG, said carrier being produced by the method of claim 26.

28. A method for delivering a substance to the interior of a cell, said substance being bonded to or incorporated in the carrier of claim 25 that has been modified with the peptide chemically modified with PEG.